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<110> APARICIO, SAMUEL
CARLTON, MARK
MITCHELL, PHILIP

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<141> 2004-04-16

<150> PCT/GB02/04725

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<151> 2001-10-24

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<151> 2001-10-19

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<170> PatentIn Ver. 3.2

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Phe	Cys	Ile	Pro	Val	Thr	Met	Leu	Gln	Asn	Ile	Ser	Asp	Lys	Trp	Leu	100	105	110	
Gly	Gly	Ala	Phe	Ile	Cys	Lys	Met	Val	Pro	Phe	Val	Gln	Ser	Thr	Ala	115	120	125	
Val	Val	Thr	Glu	Ile	Leu	Thr	Met	Thr	Cys	Ile	Ala	Val	Glu	Arg	His	130	135	140	
Gln	Gly	Leu	Ile	His	Pro	Phe	Lys	Met	Lys	Trp	Gln	Tyr	Thr	Thr	Arg	145	150	155	160
Arg	Ala	Phe	Thr	Ile	Leu	Gly	Val	Val	Trp	Leu	Ala	Ala	Ile	Ile	Val	165	170	175	
Gly	Ser	Pro	Met	Trp	His	Val	Gln	Arg	Leu	Glu	Ile	Lys	Tyr	Asp	Phe	180	185	190	
Leu	Tyr	Glu	Lys	Glu	His	Val	Cys	Cys	Leu	Glu	Glu	Trp	Ala	Ser	Pro	195	200	205	
Met	His	Gln	Arg	Ile	Tyr	Thr	Thr	Phe	Ile	Leu	Val	Ile	Leu	Phe	Leu	210	215	220	
Leu	Pro	Leu	Val	Val	Met	Leu	Val	Leu	Tyr	Ser	Lys	Ile	Gly	Tyr	Glu	225	230	235	240
Leu	Trp	Ile	Lys	Lys	Arg	Val	Gly	Asp	Ser	Ser	Ala	Leu	Gln	Thr	Ile	245	250	255	
His	Gly	Lys	Glu	Met	Ser	Lys	Ile	Ala	Arg	Lys	Lys	Lys	Arg	Ala	Val	260	265	270	
Val	Met	Met	Val	Thr	Val	Val	Ala	Leu	Phe	Ala	Ala	Cys	Trp	Ala	Pro	275	280	285	
Phe	His	Val	Val	His	Met	Met	Val	Glu	Tyr	Ser	Asn	Phe	Glu	Lys	Glu	290	295	300	
Tyr	Asp	Asp	Val	Thr	Ile	Lys	Met	Val	Phe	Ala	Val	Ala	Gln	Thr	Ile	305	310	315	320
Gly	Phe	Phe	Asn	Ser	Ile	Cys	Asn	Pro	Phe	Val	Tyr	Ala	Phe	Met	Asn				

<212> DNA
<213> Homo sapiens

<400> 13

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ccgggagcgc ccaagctggc cctcgtgctc accggcgtgc tcattcttcg cctggcgctc 180
tttggcaatg ctctggtggt ctacgtggtg accgcagca aggccatgcg caccgtcacc 240
aacatcttta tctgctcctt ggcgctcagt gacctgctca tcaccttctt ctgcattccc 300
gtcaccatgc tccagaacat ttccgacaac tggctggggg gtgctttcat ttgcaagatg 360
gtgccatttg tccagtctac cgctgtttgt acagaaatcc tcactatgac ctgcattgct 420
gtggaaaggc accagggact tgtgcatcct tttaaaatga agtggcaata caccaaccga 480
agggctttca caatgctagg tgtggtctgg ctggtggcag tcatcgtagg atcacccatg 540
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tgcttagaag agtggaccag ccctgtgcac cagaagatct acaccacctt catccttgtc 660
atcctcttcc tcctgcctct tatggtgatg cttattctgt acagtaaaat tggttatgaa 720
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atgtccaaaa tagccaggaa gaagaaacga gctgtcatta tgatggtgac agtgggtggc 840
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aggcatggaa attcaggaat tacaatgatg cggaagaaag caaagtttct cctcagagag 1140
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<210> 14
<211> 457
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
fusion protein construct

<400> 14

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Asp His Asn Leu Thr Arg Glu Gln Phe Ile Ala Leu Tyr Arg Leu Arg
                20                      25                      30

Pro Leu Val Tyr Thr Pro Glu Leu Pro Gly Arg Ala Lys Leu Ala Leu
                35                      40                      45

Val Leu Thr Gly Val Leu Ile Phe Ala Leu Ala Leu Phe Gly Asn Ala
 50                      55                      60

Leu Val Phe Tyr Val Val Thr Arg Ser Lys Ala Met Arg Thr Val Thr
 65                      70                      75                      80

Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser Asp Leu Leu Ile Thr Phe
                85                      90                      95

Phe Cys Ile Pro Val Thr Met Leu Gln Asn Ile Ser Asp Asn Trp Leu
                100                      105                      110

Gly Gly Ala Phe Ile Cys Lys Met Val Pro Phe Val Gln Ser Thr Ala
 115                      120                      125
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Val	Val	Thr	Glu	Ile	Leu	Thr	Met	Thr	Cys	Ile	Ala	Val	Glu	Arg	His	130	135	140
Gln	Gly	Leu	Val	His	Pro	Phe	Lys	Met	Lys	Trp	Gln	Tyr	Thr	Asn	Arg	145	150	155
Arg	Ala	Phe	Thr	Met	Leu	Gly	Val	Val	Trp	Leu	Val	Ala	Val	Ile	Val	165	170	175
Gly	Ser	Pro	Met	Trp	His	Val	Gln	Gln	Leu	Glu	Ile	Lys	Tyr	Asp	Phe	180	185	190
Leu	Tyr	Glu	Lys	Glu	His	Ile	Cys	Cys	Leu	Glu	Glu	Trp	Thr	Ser	Pro	195	200	205
Val	His	Gln	Lys	Ile	Tyr	Thr	Thr	Phe	Ile	Leu	Val	Ile	Leu	Phe	Leu	210	215	220
Leu	Pro	Leu	Met	Val	Met	Leu	Ile	Leu	Tyr	Ser	Lys	Ile	Gly	Tyr	Glu	225	230	235
Leu	Trp	Ile	Lys	Lys	Arg	Val	Gly	Asp	Gly	Ser	Val	Leu	Arg	Thr	Ile	245	250	255
His	Gly	Lys	Glu	Met	Ser	Lys	Ile	Ala	Arg	Lys	Lys	Lys	Arg	Ala	Val	260	265	270
Ile	Met	Met	Val	Thr	Val	Val	Ala	Leu	Phe	Ala	Val	Cys	Trp	Ala	Pro	275	280	285
Phe	His	Val	Val	His	Met	Met	Ile	Glu	Tyr	Ser	Asn	Phe	Glu	Lys	Glu	290	295	300
Tyr	Asp	Asp	Val	Thr	Ile	Lys	Met	Ile	Phe	Ala	Ile	Val	Gln	Ile	Ile	305	310	315
Gly	Phe	Ser	Asn	Ser	Ile	Cys	Asn	Pro	Ile	Val	Tyr	Ala	Phe	Met	Asn	325	330	335
Glu	Asn	Phe	Lys	Lys	Asn	Val	Leu	Ser	Ala	Val	Cys	Tyr	Cys	Ile	Val	340	345	350
Asn	Lys	Thr	Phe	Ser	Pro	Ala	Gln	Arg	His	Gly	Asn	Ser	Gly	Ile	Thr	355	360	365
Met	Met	Arg	Lys	Lys	Ala	Lys	Phe	Ser	Leu	Arg	Glu	Asn	Pro	Val	Glu	370	375	380
Glu	Thr	Lys	Gly	Glu	Ala	Phe	Ser	Asp	Gly	Asn	Ile	Glu	Val	Lys	Leu	385	390	395
Cys	Glu	Gln	Thr	Glu	Glu	Lys	Lys	Lys	Leu	Lys	Arg	His	Leu	Ala	Leu	405	410	415
Phe	Arg	Ser	Glu	Leu	Ala	Glu	Asn	Ser	Pro	Leu	Asp	Ser	Gly	Gln	Arg	420	425	430
Ala	Ile	Arg	Glu	Leu	Gly	Lys	Pro	Ile	Pro	Asn	Pro	Leu	Leu	Gly	Leu	435	440	445

Asp Ser Ser His His His His His His
450 455

<210> 15
<211> 1311
<212> DNA
<213> Homo sapiens

<400> 15
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ccagagctgc cgggacgcgc caagctggcc ctcgctgctca ccggcgtgct catcttcgcc 180
ctggcgctct ttggcaatgc tctgggtgttc taogtgggtga ccgcagcaa ggccatgcgc 240
accgtcacca acatctttat ctgctccttg gcgctcagtg acctgctcat caccttcttc 300
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accaaccgaa gggctttcac aatgctaggt gtgggtctggc tgggtggcagt catcgtagga 540
tcacccatgt ggcacgtgca acaacttgag atcaaataatg acttcctata tgaaaaggaa 600
cacatctgct gcttagaaga gtggaccagc cctgtgcacc agaagatcta caccaccttc 660
atccttgctca tcctcttcct cctgcctcct atgggtgatgc ttattctgta cagtaaaatt 720
ggttatgaac tttggataaa gaaaagagtt ggggatgggt cagtgcctcg aactattcat 780
ggaaaagaaa tgtccaaaat agccaggaag aagaaacgag ctgtcattat gatggtgaca 840
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gtcaaattgt gtgaacagac agaggagaag aaaaagctca aacgacatct tgctctcttt 1260
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<210> 16
<211> 1335
<212> DNA
<213> Homo sapiens

<400> 16
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ccagagctgc cgggacgcgc caagctggcc ctcgctgctca ccggcgtgct catcttcgcc 180
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accaaccgaa gggctttcac aatgctaggt gtgggtctggc tgggtggcagt catcgtagga 540
tcacccatgt ggcacgtgca acaacttgag atcaaataatg acttcctata tgaaaaggaa 600
cacatctgct gcttagaaga gtggaccagc cctgtgcacc agaagatcta caccaccttc 660
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gataagtaag gatcc 1335

<210> 17
<211> 439
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
fusion construct

<400> 17
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Asp His Asn Leu Thr Arg Glu Gln Phe Ile Ala Leu Tyr Arg Leu Arg
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Pro Leu Val Tyr Thr Pro Glu Leu Pro Gly Arg Ala Lys Leu Ala Leu
35 40 45
Val Leu Thr Gly Val Leu Ile Phe Ala Leu Ala Leu Phe Gly Asn Ala
50 55 60
Leu Val Phe Tyr Val Val Thr Arg Ser Lys Ala Met Arg Thr Val Thr
65 70 75 80
Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser Asp Leu Leu Ile Thr Phe
85 90 95
Phe Cys Ile Pro Val Thr Met Leu Gln Asn Ile Ser Asp Asn Trp Leu
100 105 110
Gly Gly Ala Phe Ile Cys Lys Met Val Pro Phe Val Gln Ser Thr Ala
115 120 125
Val Val Thr Glu Ile Leu Thr Met Thr Cys Ile Ala Val Glu Arg His
130 135 140
Gln Gly Leu Val His Pro Phe Lys Met Lys Trp Gln Tyr Thr Asn Arg
145 150 155 160
Arg Ala Phe Thr Met Leu Gly Val Val Trp Leu Val Ala Val Ile Val
165 170 175
Gly Ser Pro Met Trp His Val Gln Gln Leu Glu Ile Lys Tyr Asp Phe
180 185 190
Leu Tyr Glu Lys Glu His Ile Cys Cys Leu Glu Glu Trp Thr Ser Pro
195 200 205
Val His Gln Lys Ile Tyr Thr Thr Phe Ile Leu Val Ile Leu Phe Leu
210 215 220
Leu Pro Leu Met Val Met Leu Ile Leu Tyr Ser Lys Ile Gly Tyr Glu
225 230 235 240
Leu Trp Ile Lys Lys Arg Val Gly Asp Gly Ser Val Leu Arg Thr Ile
245 250 255

His Gly Lys Glu Met Ser Lys Ile Ala Arg Lys Lys Lys Arg Ala Val
 260 265 270
 Ile Met Met Val Thr Val Val Ala Leu Phe Ala Val Cys Trp Ala Pro
 275 280 285
 Phe His Val Val His Met Met Ile Glu Tyr Ser Asn Phe Glu Lys Glu
 290 295 300
 Tyr Asp Asp Val Thr Ile Lys Met Ile Phe Ala Ile Val Gln Ile Ile
 305 310 315 320
 Gly Phe Ser Asn Ser Ile Cys Asn Pro Ile Val Tyr Ala Phe Met Asn
 325 330 335
 Glu Asn Phe Lys Lys Asn Val Leu Ser Ala Val Cys Tyr Cys Ile Val
 340 345 350
 Asn Lys Thr Phe Ser Pro Ala Gln Arg His Gly Asn Ser Gly Ile Thr
 355 360 365
 Met Met Arg Lys Lys Ala Lys Phe Ser Leu Arg Glu Asn Pro Val Glu
 370 375 380
 Glu Thr Lys Gly Glu Ala Phe Ser Asp Gly Asn Ile Glu Val Lys Leu
 385 390 395 400
 Cys Glu Gln Thr Glu Glu Lys Lys Lys Leu Lys Arg His Leu Ala Leu
 405 410 415
 Phe Arg Ser Glu Leu Ala Glu Asn Ser Pro Leu Asp Ser Gly His Asp
 420 425 430
 Tyr Lys Asp Asp Asp Asp Lys
 435

<210> 18
 <211> 7200
 <212> DNA
 <213> Mus musculus

<220>
 <221> CDS
 <222> (2004)..(2345)

<400> 18
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 aggggatctg tctgtgcaca ggaagaagcg aaatatgaag gagtaaggag agcaggggtg 180
 gggggcagcg atggagggga acgagtaaga aaaaccataa agacacatgc tatgaaaatg 240
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aaagtccagc	gacccctactg	agatcaccac	aggtcatta	gcaccgctag	ggtttttaact	660										
agatgggctg	tgtgggtaag	acagcttcat	ttgcaatcaa	gagggtcagg	gttaaccaa	720										
gaatctacat	aagaagcaag	ccatgcctct	gtccaacacc	cctcccctac	actgtgtctta	780										
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Phe	Ser	Arg	Leu	Leu	Ser	Ala	His	Asn	Leu	Thr	Arg	Glu	Gln	Phe	Ile	
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His Arg Tyr Gly Leu Arg Pro Leu Val Tyr Thr Pro Glu Leu Pro Ala	
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cgc gct aaa ctg gcc ttt gcg ctg gct gga gca ctc att ttt gcc ctg	2177
Arg Ala Lys Leu Ala Phe Ala Leu Ala Gly Ala Leu Ile Phe Ala Leu	
45 50 55	
gcg ctc ttt ggc aac tct ctg gtc atc tat gtg gtg acc ccg agc aag	2225
Ala Leu Phe Gly Asn Ser Leu Val Ile Tyr Val Val Thr Arg Ser Lys	
60 65 70	
gcc atg cgc acc gtc acc aac atc ttc atc tgc tct ctg gca ctc agt	2273
Ala Met Arg Thr Val Thr Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser	
75 80 85 90	
gat ctg ctc att gcc ttc ttc tgc atc ccc gtc acg atg ctc cag aac	2321
Asp Leu Leu Ile Ala Phe Phe Cys Ile Pro Val Thr Met Leu Gln Asn	
95 100 105	
atc tcc gac aag tgg ctg ggt ggt aagacagcga ttacgcgtgc aactcacgg	2375
Ile Ser Asp Lys Trp Leu Gly Gly	
110	
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cctggtaacc ctgtagacaa aaactgtggt gggggatggg ggtttgccct tacagttcag	2555
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7200

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<212> PRT

<213> Mus musculus

<400> 19

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			20					25					30		

Pro	Leu	Val	Tyr	Thr	Pro	Glu	Leu	Pro	Ala	Arg	Ala	Lys	Leu	Ala	Phe
		35					40					45			

Ala	Leu	Ala	Gly	Ala	Leu	Ile	Phe	Ala	Leu	Ala	Leu	Phe	Gly	Asn	Ser
	50					55					60				

Leu	Val	Ile	Tyr	Val	Val	Thr	Arg	Ser	Lys	Ala	Met	Arg	Thr	Val	Thr
65					70					75					80

Asn	Ile	Phe	Ile	Cys	Ser	Leu	Ala	Leu	Ser	Asp	Leu	Leu	Ile	Ala	Phe
				85					90					95	

Phe	Cys	Ile	Pro	Val	Thr	Met	Leu	Gln	Asn	Ile	Ser	Asp	Lys	Trp	Leu
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Gly Gly

<210> 20

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: 6-His tag

<400> 20

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<210> 21

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 21

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27

<210> 22
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 <212> DNA
 <213> Artificial Sequence

 <220>
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 <400> 22
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<210> 23
 <211> 31
 <212> DNA
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 <220>
 <223> Description of Artificial Sequence: PCR primer

 <400> 23
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<210> 24
 <211> 37
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Description of Artificial Sequence: PCR primer

 <400> 24
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<210> 25
 <211> 36
 <212> DNA
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 <220>
 <223> Description of Artificial Sequence: PCR primer

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<210> 26
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 <212> DNA
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<210> 28
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 <212> DNA
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 <220>
 <223> Description of Artificial Sequence: PCR primer

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<210> 29
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<210> 30
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 <210> 34
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 <210> 35
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 <400> 35
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 <210> 36
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<212> DNA

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<213> Homo sapiens

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Thr Pro Thr Asn Ile Phe Ile Leu Asn Leu Ala Val Ala Asp Leu Leu
20 25 30

Phe Leu Leu Thr Leu Pro Pro Trp Ala Leu Tyr Tyr Leu Val Gly Gly
35 40 45

Ser Glu Asp Trp Pro Phe Gly Ser Ala Leu Cys Lys Leu Val Thr Ala
50 55 60

Leu Asp Val Val Asn Met Tyr Ala Ser Ile Leu Leu Thr Ala Ile
65 70 75 80

Ser Ile Asp Arg Tyr Leu Ala Ile Val His Pro Leu Arg Tyr Arg Arg
85 90 95

Arg Arg Thr Ser Pro Arg Arg Ala Lys Val Val Ile Leu Leu Val Trp
100 105 110

Val Leu Ala Leu Leu Leu Ser Leu Pro Pro Leu Leu Phe Ser Trp Val

115						120						125					
Lys	Thr	Val	Glu	Glu	Gly	Asn	Gly	Thr	Leu	Asn	Val	Asn	Val	Thr	Val		
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Cys	Leu	Ile	Asp	Phe	Pro	Glu	Glu	Ser	Thr	Ala	Ser	Val	Ser	Thr	Trp		
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165						170						175					
Leu	Leu	Val	Ile	Leu	Val	Cys	Tyr	Thr	Arg	Ile	Leu	Arg	Thr	Leu	Arg		
180						185						190					
Lys	Arg	Ala	Arg	Lys	Gly	Ala	Ser	Lys	Lys	Arg	Ser	Ser	Lys	Glu	Arg		
195						200						205					
Lys	Ala	Ala	Lys	Thr	Leu	Leu	Val	Val	Val	Val	Val	Phe	Val	Leu	Cys		
210						215						220					
Trp	Leu	Pro	Tyr	Phe	Ile	Val	Leu	Leu	Leu	Asp	Thr	Leu	Cys	Leu	Ser		
225						230						235					
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245						250						255					
Leu	Leu	Val	Thr	Leu	Trp	Leu	Ala	Tyr	Val	Asn	Ser	Cys	Leu	Asn	Pro		
260						265						270					
Ile	Ile	Tyr															
275																	